=> fil hcaplu
FILE 'HCAPLUS' ENTERED AT 15:24:14 ON 07 NOV 2002
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FILE COVERS 1907 - 7 Nov 2002 VOL 137 ISS 19
FILE LAST UPDATED: 6 Nov 2002 (20021106/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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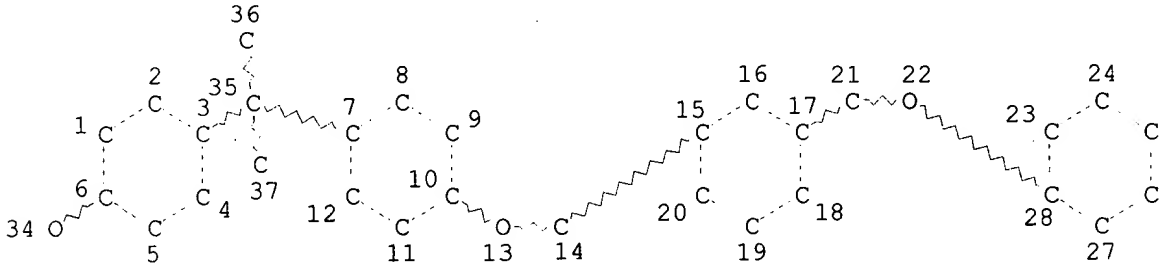
L3 STR



Page 1-A

25

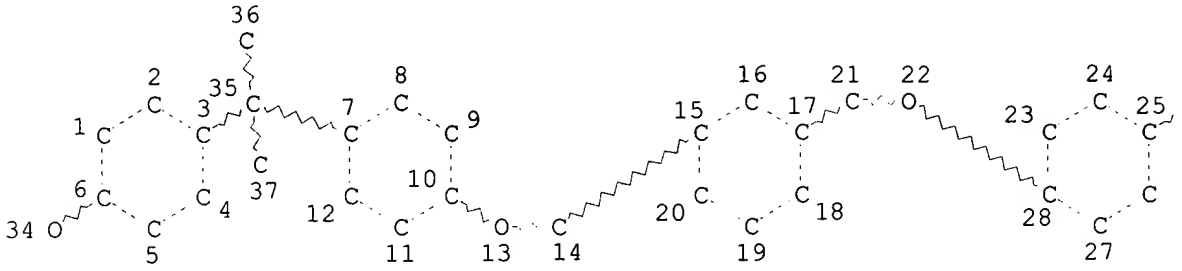
26

Page 1-B
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 32

Searched by M. Smith

STEREO ATTRIBUTES: NONE
L5 62 SEA FILE=REGISTRY SSS FUL L3
L6 STR



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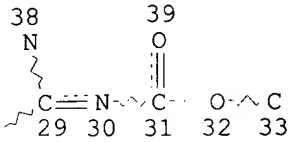

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Page 1-B
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 39

STEREO ATTRIBUTES: NONE
L7 2 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L8 6 SEA FILE=HCAPLUS L7

=> d ibib abs hitrn l8 1-6

L8 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:594844 HCAPLUS
DOCUMENT NUMBER: 137:140518
TITLE: Preparation of thiazolyl-, oxazolyl-, pyrrolyl-, and imidazolyl- acid amide derivatives as inhibitors of phosphodiesterase IV isozymes
INVENTOR(S): Marfat, Anthony; McKechney, Michael William
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 249 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

Weddington 09/889,409 /p

WO 2002060898 A1 20020808 WO 2001-IB2728 20011224
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002123520 A1 20020905 US 2002-62145 20020131
PRIORITY APPLN. INFO.: US 2001-265486P P 20010131
OTHER SOURCE(S): MARPAT 137:140518
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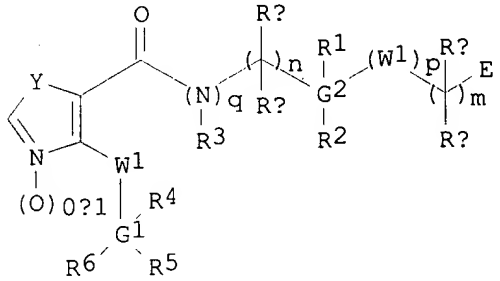

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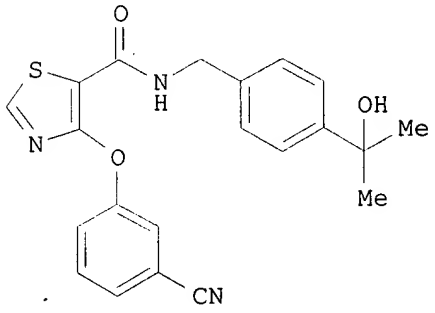

II

AB Title compds. I [wherein p = 0-1; q = 0-1; provided that when q = 0, n = 2; m = 0-3; n = 1-2; W1 and W2 = independently O, SO0-2, or NR3; or W2 = (un)substituted methylene; Y = SO0-2, O, NO0-1, NR3, or (un)substituted methylene; ; RA and RB = independently H, F, CF3, alkyl, or (un)substituted cycloalkyl, Ph, or benzyl; or when m = 1, CRARB = (un)substituted spiro; RC and RD have the same meaning as RA and RB except that one of them must be H; R1 and R2 = H, F, Cl, CN, NO2, (fluoro)alkyl, alkynyl, alkoxy, phenoxy, carbamoyl, etc.; R3 = H, alkyl, Ph, benzyl, alkoxy, phenoxy, etc.; R4, R5, and R6 = H, F, Cl, and (un)substituted (cyclo)alkyl, alkenyl, alkynyl, Ph, benzyl, pyridyl, alkoxy, phenoxy, acyl, carboxy, CN, NO2, carbamoyl, ureido, (hetero)aryl, etc.; G1 and G2 = independently (un)satd. carbocyclyl or heterocyclyl; E = (un)substituted carboxy, carbamoyl, acyl, hydroxyalkyl, cyanoalkyl, acylamino, ureido, amino, heterocyclyl, etc.] were prepd. as inhibitors of PDE4 (no data). For example, 4-(3-cyanophenoxy)thiazole-5-carboxylic acid was treated with 2-(4-aminomethylphenyl)propan-2-ol in the presence of EDCl and HOBT in DMF

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to give the thiazolamide II. I are useful in the treatment of diseases regulated by the activation and degranulation of eosinophils, esp. asthma, chronic bronchitis, and chronic obstructive pulmonary disease (no data). In addn., I may be used in combination therapy with a wide variety of other therapeutic agents.

IT **346735-24-8**, BIIL 284
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy with PDE4 inhibitors; prepn. of thiazolyl-, oxazolyl-, pyrrolyl-, and imidazolyl- acid amide derivs. as inhibitors of PDE4 isoenzymes)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:594842 HCAPLUS
DOCUMENT NUMBER: 137:154859
TITLE: Preparation of carbamoyl-substituted pyridinyl aryl ether derivatives as inhibitors of phosphodiesterase IV isozymes
INVENTOR(S): Chambers, Robert James; Magee, Thomas Victor; Marfat, Anthony
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060896	A1	20020808	WO 2001-IB2726	20011224

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-265304P P 20010131
OTHER SOURCE(S): MARPAT 137:154859
GI

Searched by M. Smith

Weddington 09/889,409 /p

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 6 NOV 2002 HIGHEST RN 471238-76-3
DICTIONARY FILE UPDATES: 6 NOV 2002 HIGHEST RN 471238-76-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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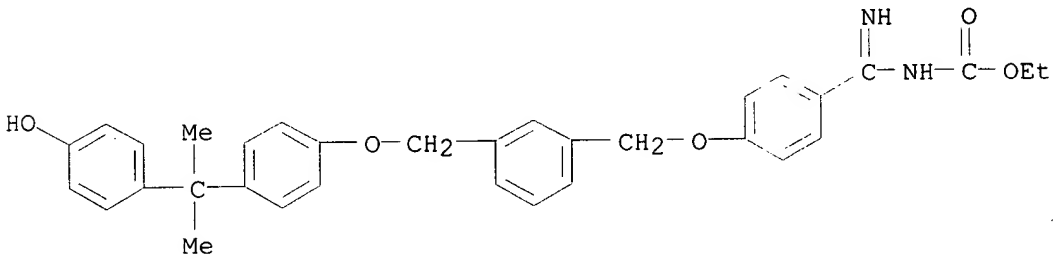
L7 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN 349542-91-2 REGISTRY
CN Carbamic acid, [[4-[[3-[[4-[1-(4-hydroxyphenyl)-1-methylethyl]phenoxy]methyl]phenyl]methoxy]phenyl]iminomethyl]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)
MF C33 H34 N2 O5 . Cl H
SR CA
LC STN Files: CA, CAPLUS, CASREACT, DRUGUPDATES, USPAT2, USPATFULL
CRN (346735-24-8)



● HCl

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

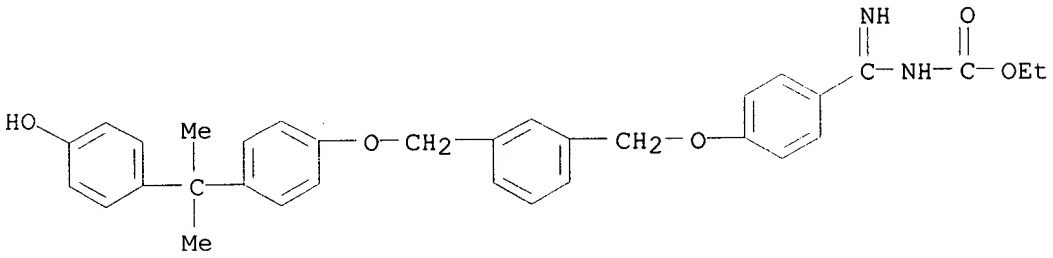
REFERENCE 1: 135:107153

L7 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN 346735-24-8 REGISTRY
CN Carbamic acid, [[4-[[3-[[4-[1-(4-hydroxyphenyl)-1-methylethyl]phenoxy]methyl]phenyl]methoxy]phenyl]iminomethyl]-, ethyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Amelubant
CN BIIL 284

Searched by M. Smith

Weddington 09/889,409 /p

FS 3D CONCORD
MF C33 H34 N2 O5
CI COM
SR CA
LC STN Files: CA, CAPLUS, CASREACT, DRUGNL, DRUGUPDATES, PHAR, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

6 REFERENCES IN FILE CA (1962 TO DATE)
6 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:154859

REFERENCE 2: 137:140518

REFERENCE 3: 137:140509

REFERENCE 4: 137:103921

REFERENCE 5: 135:107153

REFERENCE 6: 135:70889

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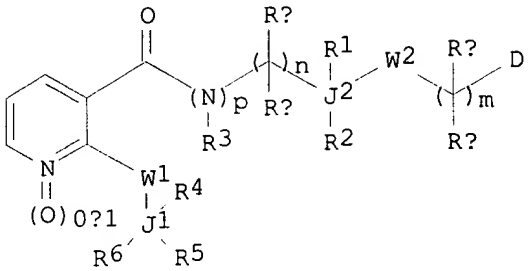

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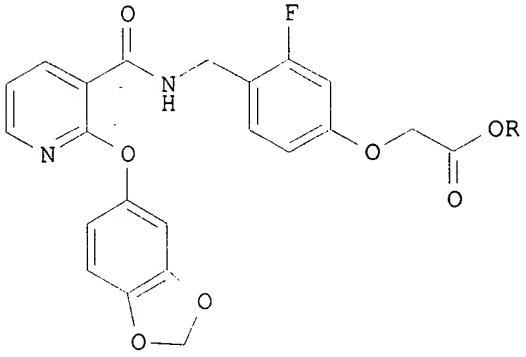


II

AB Title compds. compds. I [wherein p = 0-1, provided that when p = 0, n = 2; m = 1-3; n = 1-2; W1 and W2 = independently O, S(O)0-2, or NR3; Y = =C(R1a) or N(O)0-1; R1a = H, F, Cl, CN, NO2, (fluoro)alkyl, alkynyl, fluoroalkoxy, OR16, or (un)substituted carbamoyl; RA and RB = independently H, F, CF3, or (un)substituted (cyclo)alkyl, Ph, or benzyl; or CRARB = spiro moiety; RC and RD = the same as RA and RB except that one of them must be H; R1 and R2 = independently H, F, Cl, CN, NO2, (fluoro)alkyl, alkynyl, OR16, or (un)substituted carbamoyl; R3 = H, alkyl, Ph, benzyl, or OR16; R4, R5 and R6 = independently H, F. Cl, alkynyl, R16, OR16, SO0-2R16, COR16, CO2R16, OCOR16, CN, NO2, (un)substituted carbamoyl(oxy), ureido, carboximidoyl, aryl, heterocyclyl, etc.; or R5 and R6 taken together with the atoms to which they are attached = (hetero)cyclyl; J1 and J2 = independently (un)substituted, (un)satd. monocyclic or fused polycyclic ring; D = (un)substituted carboxy, carbamoyl, acyl, hydroxy(alkyl), cyano(alkyl), etc.; R16 = H or (un)substituted (cyclo)alkyl, alkenyl, Ph, benzyl, or pyridyl] were prepd. as inhibitors of PDE4 (no data). For example, 2-(benzo[1,3]dioxol-5-yloxy)nicotinic acid was coupled with (4-aminomethyl-3-fluorophenoxy)acetic acid Me ester in the presence of 1-hydroxybenzotriazole.bul.H2O and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide.bul.HCl in DMF/CH2Cl2 to give the pyridinecarboxamide II (R = Me) in 38% yield. Sapon. using aq. LiOH in THF and MeOH afforded the desired acid II (R = OH) in 21% yield. I are useful in the treatment of diseases regulated by the activation and degranulation of eosinophils, esp. asthma, chronic bronchitis, and chronic obstructive pulmonary disease (no data). In addn., I may be used in combination therapy with a wide variety of other therapeutic agents.

IT **346735-24-8**, BIIL 284
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy with PDE4 inhibitors; prepn. of

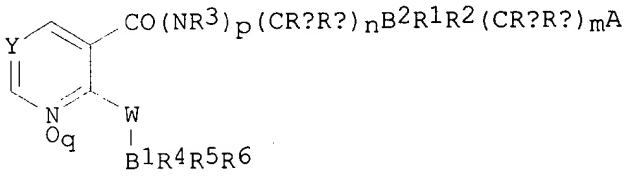
carbamoyl-substituted pyridinyl aryl ether derivs. as inhibitors of PDE4 isoenzymes)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:591707 HCAPLUS
DOCUMENT NUMBER: 137:140509
TITLE: Preparation of nicotinamides and mimetics as inhibitors of phosphodiesterase IV isozymes
INVENTOR(S): Chambers, Robert J.; Magee, Thomas V.; Marfat, Anthony
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 180 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1229034	A1	20020807	EP 2002-250202	20020111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002111495	A1	20020815	US 2002-62811	20020131

PRIORITY APPLN. INFO.: US 2001-265240P P 20010131
US 1997-43403P P 19970404
US 1998-105120P P 19981021

OTHER SOURCE(S): MARPAT 137:140509
GI



I

AB Title compds. [I; p, q = 0, 1; m = 0-2; n = 1, 2; A = CO2R7, CONR9CO2R7, CONR7R9, OP(O)(OH)2, SO3H, acylsulfonamido, etc.; W = O, S, SO, SO2, NR3; Y = N, NO, CR11; R1, R2 = H, F, Cl, cyano, NO2, alkyl, alkynyl, fluoroalkyl, etc.; R3 = H, alkyl, Ph, PhCH2, etc.; R4-R6 = H, F, Cl, alkynyl, cyano, NO2, etc.; R7 = H, (substituted) alkyl, alkenyl, alkynyl; R9 = H, alkyl, cycloalkyl, Ph, PhCH2, pyridyl, etc.; R11 = H, F, Cl, cyano, NO2, alkyl, alkynyl, fluoroalkyl, fluoroalkoxy, etc.; Ra, Rb = H, F, CF3, alkyl, (substituted) cycloalkyl, Ph, PhCH2; B1, B2 = 3-7 membered (hetero)cyclyl, 7-12 membered poly(hetero)cyclyl; pairs of variables may form rings; with provisos], were prepd. (no data). Thus, Me 2-[4-[[[2-(benzo[1,3]dioxol-5-yloxy)pyridine-3-carbonyl]amino]methyl]phenyl]-2-methylpropionate was suspended in Me3COH. Aq. NaOH was added to the suspension, and the reaction mixt. was refluxed 1 h to give 2-[4-[[[2-(benzo[1,3]dioxol-5-yloxy)pyridine-3-carbonyl]amino]methyl]phenyl]-2-methylpropionic acid.

IT **346735-24-8**, BIIL 284
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; prepn. of nicotinamides and mimetics as

inhibitors of phosphodiesterase IV isoenzymes)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:539517 HCAPLUS
DOCUMENT NUMBER: 137:103921
TITLE: Use of an LTB4 antagonist for the treatment and/or prevention of diseases caused by increased expression of mucin genes
INVENTOR(S): Anderskewitz, Ralf; Meade, Christopher John Montague; Birke, Franz; Jennewein, Hans Michael; Jung, Birgit
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma KG, Germany
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055065	A2	20020718	WO 2002-EP309	20020115
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002137792	A1	20020926	US 2002-50409	20020116

PRIORITY APPLN. INFO.: GB 2001-1128 A 20010116
US 2001-266833P P 20010206

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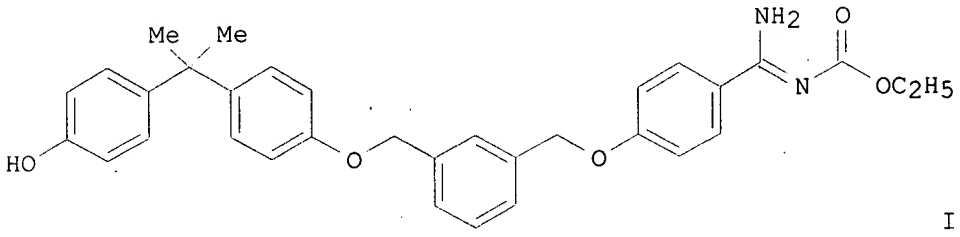

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AB The invention discloses the use of LTB4 antagonist I or a pharmaceutically acceptable salt thereof for the prepn. of a medicament for the treatment and/or prevention of diseases caused by increased expression of mucin genes and/or hyperplasia of goblet cells induced by toxins of products of pathogenic bacteria in the bronchial or gastrointestinal epithelium.

IT **346735-24-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LTB4 antagonist for treatment and/or prevention of diseases caused by

increased expression of mucin genes)

L8 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:523500 HCAPLUS
DOCUMENT NUMBER: 135:107153
TITLE: Procedure for the production of aryl iminomethyl carbamic acid esters
INVENTOR(S): Brandenburg, Joerg; Soyka, Rainer; Schmid, Rolf; Anderskewitz, Ralf; Bauer, Rolf; Hamm, Rainer; Kroeber, Jutta
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10000907	A1	20010719	DE 2000-10000907	20000112
US 2001009958	A1	20010726	US 2001-757253	20010109
US 6417382	B2	20020709		
WO 2001051457	A2	20010719	WO 2001-EP262	20010111
WO 2001051457	A3	20020117		
W: AE, AU, BG, BR, CA, CN, CZ, EE, HU, ID, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1250318	A2	20021023	EP 2001-942357	20010111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				
US 2002137963	A1	20020926	US 2002-138955	20020505

PRIORITY APPLN. INFO.:
DE 2000-10000907 A 20000112
US 2000-177378P P 20000124
US 2001-757253 A1 20010109
WO 2001-EP262 W 20010111

OTHER SOURCE(S): CASREACT 135:107153; MARPAT 135:107153
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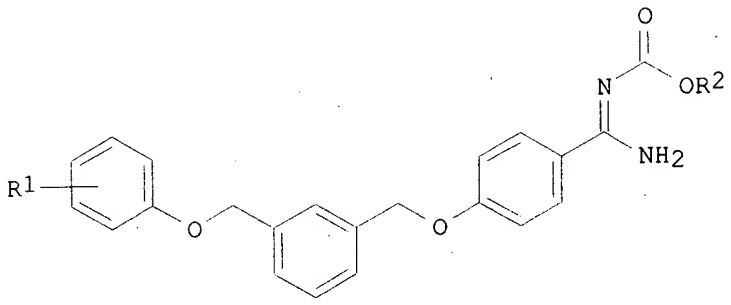
Searched by M. Smith



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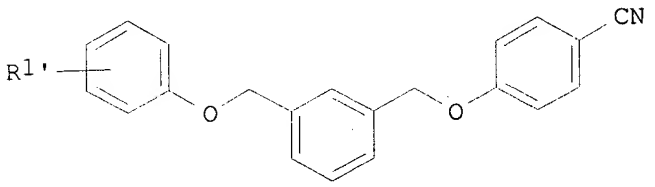

II

AB The title compds. [I; C1-3 alkyl, cyclopentyl, cyclohexyl, Ph, PhCH2, (un)substituted C(CH3)2Ph; R2 = C1-3 alkyl, PhCH2] [e.g., Et [[4-[3-[4-[1-(4-hydroxyphenyl)-1-methylethyl]phenoxymethyl]benzyloxy]phenyl]iminomethyl]carbamate] are prepd. in high yield by the reaction of benzonitriles (II) in an arom. or ether solvent with lithium bis(trimethylsilyl)amide, sodium bis(trimethylsilyl)amide, or potassium bis(trimethylsilyl)amide, followed by reaction of the intermediate with carbonate ester halide R2O2CX (X = Cl, Br, OR2) followed by treatment with aq. HCl to give a hydrochloride salt of I.

IT **346735-24-8P**
RL: IMF (Industrial manufacture); PREP (Preparation)
(procedure for the prodn. of aryl iminomethyl carbamic acid esters)

IT **349542-91-2P**
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(procedure for the prodn. of aryl iminomethyl carbamic acid esters)

L8 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:240859 HCAPLUS
DOCUMENT NUMBER: 135:70889
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AB BIIL 284 is a new LTB4 receptor antagonist. It is a prodrug and has

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negligible binding to the LTB4 receptor. However, ubiquitous esterases metabolize BIIL 284 to the active metabolites BIIL 260 and BIIL 315, the glucuronidated form of BIIL 260. Both metabolites have high affinity to the LTB4 receptor on isolated human neutrophil cell membranes with Ki values of 1.7 and 1.9 nM, resp. On vital human neutrophilic granulocytes Ki was around 1 nM. BIIL 260 and BIIL 315 interact with the LTB4 receptor in a saturable, reversible, and competitive manner. BIIL 260 and its glucuronide BIIL 315 also potently inhibited LTB4-induced intracellular Ca2+ release in human neutrophils (IC50 values of 0.82 and 0.75 nM, resp.) as measured with Fura-2. High efficacy of BIIL 284 has been demonstrated in various in vivo models. BIIL 284 inhibited LTB4-induced mouse ear inflammation with ED50 = 0.008 mg/kg p.o., LTB4-induced transdermal chemotaxis in guinea pigs with ED50 = 0.03 mg/kg p.o., LTB4-induced neutropenia in various species (monkey: ED50 = 0.004 mg/kg p.o.), and LTB4-induced Mac1-expression in monkeys (ED50 = 0.05 mg/kg p.o. in Tylose). Full blockade of LTB4 receptors over 24 h was achieved by 0.3 mg/kg BIIL 284 after single oral dose as measured by LTB4-induced neutropenia or Mac1-expression in the monkey model. BIIL 284 is an unusually potent and long-acting orally active LTB4 antagonist, and is therefore under clin. development as a novel anti-inflammatory principle.

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(In vitro and in vivo pharmacol. characterization of BIIL 284, a novel and potent leukotriene B4 receptor antagonist)

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